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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,111	10/12/2006	Stefan Barth	3581. 10US01	1350

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DARDI & HERBERT, PLLC
Moore Lake Plaza, Suite 205
1250 East Moore Lake Drive
Fridley, MN 55432

EXAMINER	
MEAH, MOHAMMAD Y	
ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,111	BARTH ET AL.	
	Examiner	Art Unit	
	MD. YOUNUS MEAH	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19, 21, 25-26 and 29)* is/are pending in the application.

4a) Of the above claim(s) *8,9,12 and 16-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 10-11, 13-14, 15, 21, 25, 26 and 29)* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/14/06, 10/9/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election with traverse of group A_n (claims 1-7, 10-11, 13-14, 15, 21, 25, 26 and 29) comprising fusion protein comprising DAPk2 and antibody in their response of 11/16/2010 is acknowledged. Claims 8-9, 12, 16-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups. The traversal on the ground that (1) component A comprising antibody and antibody derivatives are equivalents and are not distinct from each other (2) there is no undue burden to examine all DAPk proteins in component B, and (3) restriction on the special technical feature is improper because applicant's protein is synthetic, soluble and endogenous and therefore US 5670324 art does not teach applicant's fusion complex.

Applicants' argument about component A comprising antibody and antibody derivatives which are equivalents and are not distinct from each other is found persuasive and therefore a fusion complex comprising component A comprising antibodies will be examined. Applicant's argument that there is no undue burden to examine a fusion complex comprising all DPK proteins and that the cited prior art does not teach their invention are considered but found unpersuasive. As explained in the election/restriction office action of 5/7/10 a fusion protein comprising a binding domain molecule and protein kinase is taught by Littman et al (US PAT 5670324). The fusion protein of the prior art is soluble and endogenous and could be a synthetic. Applicants further argue that there would be no undue burden on the examiner to examine claims

directed to all protein comprising DAK kinases. This is not persuasive because while the search for each of these distinct groups would be overlapping it would not be coextensive. Therefore restriction made FINAL.

Claims 1-7, 10, 13-14, 15 (for Claim 15 SEQ ID NO: 2 and 4 only), 21, 25, 26 and 29 will be examined to the extent they encompass the elected subject matter.

Claim objections

Claims 2, 6-7, 15 are objected to for comprising non-elected subject matter. Appropriate correction is required.

Claim 1 is objected for reciting "a synthetic, soluble endogenous complex....wherein the complex is synthetic, soluble and endogenous". The same limitation is recited twice. Appropriate correction is required.

Claim 2 is objected for reciting "antibody fragments synthetic peptides". It should be "antibody fragments, synthetic peptides". Appropriate correction is required.

Claim Rejections 35 U.S.C 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-7, 10, 13-14, 15, 21, 25, 26 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in reciting " synthetic—endogenous complex—" for the following reason: The term synthetic means that it is manufactured by man. The term endogenous implies that the complex is found in nature in an organism. Furthermore, the term "endogenous" is indefinite as used in the claims because the claims lack a limitation indicating the organism to which the complex is endogenous (endogenous to what? endogenous to bacteria?, endogenous to plants?, etc).

Claim 4 is indefinite for the following reason: The claim 4 recites "component A is bound to the extracellular surface structure". This term makes the claim unclear and confusing because based on the limitations of claim 1, one would understand that the extracellular surface structure is not part of the complex. The limitation in claim 4 appears to indicate that the extracellular surface structure is also part of the complex.

Claim 7 is indefinite for the recitation of the term "DAP kinase related protein kinase 1.., also named DAP-kinase 2..." This term makes the claim unclear and confusing. Does this mean that DRP-1 is the same as DAP-kinase 2?".

Claim Rejections, 35 U.S.C 112 1^{si} Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 10, 13-14, 21, 25, 26 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claim 1 is drawn to a complex formed from component A and component B, wherein component A has binding activity for cellular surface structures and component B is a protein having kinase activity. Claim 2 further limits component A to actively binding structures such as antibodies or their derivatives or fragments thereof. Claim 6 further limits component B has having eukaryotic protein kinase or histidine protein kinase, etc. or derivatives thereof. Moreover, claim 13 further limits the complex of claim 1 to encompass one or more supplementary components S in addition components A and B. Thus, the claims encompass a genus of complexes comprising components having essentially any structure and function. It is noted that derivatives of the recited components can encompass any compound which share any structural feature or any functional feature with the recited component. As such, derivatives are compounds having essentially any structure and/or function. Also, note that the genus of complexes claimed encompass (i) proteins having any structure which comprise a binding domain for any type of extracellular surface structure, and (ii) proteins having any structure which have any type of kinase activity.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied

through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099- 1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

The specification teaches (page 11) that complex of the present invention include, but are not limited to, a complex formed from at least one component A and at least one component B, wherein component A has binding activity for cellular surface structures, and component B carries a kinase as an effector function. Thus, while the specification reasonably conveys antibodies as component A, Protein kinase such as Dap-kinase as component B, and a few specific examples of component S, there is insufficient written description of the infinite number of components encompassed by the genus of complexes recited because the relevant identifying characteristics of the genus such as structure or other physical and/or chemical characteristics are not set forth in the specification as-filed. Therefore, the specification does not appear to be commensurate in full scope with the claimed invention. Vas- Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Claims 1-7, 10, 13-14, 21, 25, 26 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an fusion protein comprising SEQ ID NO: 2 or 4 (see specification page 13), does not reasonably provide enablement for any immunokinase complex formed from component A and component B, wherein component A comprise any molecule having binding activity for cellular surface structures or any antibody or derivatives or fragments thereof and component B is any kinase or eukaryotic protein kinase or histidine protein kinase, etc. wherein the complex further comprises one or more supplementary components S having any structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-7, 10, 13-14, 21, 25, 26 and 29 encompass a genus of complexes comprising components having any structure and function. Claim 1 is drawn to a complex formed from component A and component B, wherein component A has binding activity for cellular surface structures and component B is a protein having kinase activity. Claim 2 further limits component A to actively binding structures such as antibodies or their derivatives or fragments thereof. Claim 6 further limits component B has having eukaryotic protein kinase or histidine protein kinase, etc. or derivatives thereof. Moreover, claim 13 further limits the complex of claim 1 to encompass one or more supplementary components S in addition components A and B. It is noted that derivatives of the recited components can encompass any compound which share any structural feature or any functional feature with the recited component. As such,

derivatives are compounds having essentially any structure and/or function. Also, note that the genus of complexes claimed encompass (i) proteins having any structure which comprise a binding domain for any type of extracellular surface structure, and (ii) proteins having any structure which have any type of kinase activity. Thus, the claims encompass a genus of complexes comprising components having essentially any structure and function.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only few fusion proteins of specific amino acid sequences (SEQ ID NO: 2 and 4).

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to

modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any fusion protein of any antibody molecule or fragments or modified fragments thereof or derivatives thereof with any kinase protein or derivatives thereof because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting immunokinase activity; (B) the general tolerance of kinase activity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues for immunokinase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly include any complex comprising any kinase conjugated with any extracellular binding molecules or any antibody or derivatives or fragment thereof . The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of immunokinase activity, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is

unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejection - 35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7, 10-11, 13-14, 21, 25, 26 and 29 are rejected under 35 U.S.C. 102(e) as being anticipated by Lavie et al (US 7419811, claim priority on US provisional 60/451207, 25 February 2003) and Lavie et al (WO 2004/078215, claim priority on US provisional 60/451207, 25 February 2003 from IDS).

Lavie et al teach fusion protein comprising DCK kinase conjugated to antibody which bind cell surface antigen (page 5). Lavie et al teach that the fusion complex further comprises an agent like a His tag to facilitate purification of the fusion protein (column 26, lines 34-50, reads on claim 13). Lavie et al also teach that said antibody of the conjugates bind to CD antigen (CD33, column 6 lines 41-60, reads on claim 26). Claim 11 is included in the rejection because the DCK kinase of Lavie et al. is a

derivative of a DAP-kinase 2 as a derivate is a compound which shares any structural and/or functional feature with the desired compound. The kinase of Lavie et al. is structurally a homolog of a DAP-kinase 2 as well as a functional homolog of a DAP-kinase 2 as both would have kinase activity.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mohammad Younus Meah
Examiner, Art Unit 1652

/Delia M. Ramirez/
Primary Examiner, Art Unit 1652